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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/624,044	07/21/2003	Andrew J. Murphy	REG 780BZ	6377
26693	7590	10/26/2006	EXAMINER	
REGENERON PHARMACEUTICALS, INC 777 OLD SAW MILL RIVER ROAD TARRYTOWN, NY 10591			SGAGIAS, MAGDALENE K	
			ART UNIT	PAPER NUMBER
			1632	

DATE MAILED: 10/26/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

<b>Advisory Action Before the Filing of an Appeal Brief</b>	<b>Application No.</b>	<b>Applicant(s)</b>
	10/624,044	MURPHY ET AL.
	<b>Examiner</b>	<b>Art Unit</b>
	Magdalene K. Sgagias	1632

--The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

THE REPLY FILED 12 October 2006 FAILS TO PLACE THIS APPLICATION IN CONDITION FOR ALLOWANCE.

1.  The reply was filed after a final rejection, but prior to or on the same day as filing a Notice of Appeal. To avoid abandonment of this application, applicant must timely file one of the following replies: (1) an amendment, affidavit, or other evidence, which places the application in condition for allowance; (2) a Notice of Appeal (with appeal fee) in compliance with 37 CFR 41.31; or (3) a Request for Continued Examination (RCE) in compliance with 37 CFR 1.114. The reply must be filed within one of the following time periods:

- a)  The period for reply expires \_\_\_\_\_ months from the mailing date of the final rejection.  
 b)  The period for reply expires on: (1) the mailing date of this Advisory Action, or (2) the date set forth in the final rejection, whichever is later. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of the final rejection.

Examiner Note: If box 1 is checked, check either box (a) or (b). ONLY CHECK BOX (b) WHEN THE FIRST REPLY WAS FILED WITHIN TWO MONTHS OF THE FINAL REJECTION. See MPEP 706.07(f).

Extensions of time may be obtained under 37 CFR 1.136(a). The date on which the petition under 37 CFR 1.136(a) and the appropriate extension fee have been filed is the date for purposes of determining the period of extension and the corresponding amount of the fee. The appropriate extension fee under 37 CFR 1.17(a) is calculated from: (1) the expiration date of the shortened statutory period for reply originally set in the final Office action; or (2) as set forth in (b) above, if checked. Any reply received by the Office later than three months after the mailing date of the final rejection, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

#### NOTICE OF APPEAL

2.  The Notice of Appeal was filed on \_\_\_\_\_. A brief in compliance with 37 CFR 41.37 must be filed within two months of the date of filing the Notice of Appeal (37 CFR 41.37(a)), or any extension thereof (37 CFR 41.37(e)), to avoid dismissal of the appeal. Since a Notice of Appeal has been filed, any reply must be filed within the time period set forth in 37 CFR 41.37(a).

#### AMENDMENTS

3.  The proposed amendment(s) filed after a final rejection, but prior to the date of filing a brief, will not be entered because
- (a)  They raise new issues that would require further consideration and/or search (see NOTE below);
  - (b)  They raise the issue of new matter (see NOTE below);
  - (c)  They are not deemed to place the application in better form for appeal by materially reducing or simplifying the issues for appeal; and/or
  - (d)  They present additional claims without canceling a corresponding number of finally rejected claims.

NOTE: See Continuation Sheet. (See 37 CFR 1.116 and 41.33(a)).

4.  The amendments are not in compliance with 37 CFR 1.121. See attached Notice of Non-Compliant Amendment (PTOL-324).
5.  Applicant's reply has overcome the following rejection(s): \_\_\_\_\_.
6.  Newly proposed or amended claim(s) \_\_\_\_\_ would be allowable if submitted in a separate, timely filed amendment canceling the non-allowable claim(s).
7.  For purposes of appeal, the proposed amendment(s): a)  will not be entered, or b)  will be entered and an explanation of how the new or amended claims would be rejected is provided below or appended.

The status of the claim(s) is (or will be) as follows:

Claim(s) allowed: \_\_\_\_\_.

Claim(s) objected to: \_\_\_\_\_.

Claim(s) rejected: 44, 47, 53.

Claim(s) withdrawn from consideration: \_\_\_\_\_.

#### AFFIDAVIT OR OTHER EVIDENCE

8.  The affidavit or other evidence filed after a final action, but before or on the date of filing a Notice of Appeal will not be entered because applicant failed to provide a showing of good and sufficient reasons why the affidavit or other evidence is necessary and was not earlier presented. See 37 CFR 1.116(e).
9.  The affidavit or other evidence filed after the date of filing a Notice of Appeal, but prior to the date of filing a brief, will not be entered because the affidavit or other evidence failed to overcome all rejections under appeal and/or appellant fails to provide a showing a good and sufficient reasons why it is necessary and was not earlier presented. See 37 CFR 41.33(d)(1).
10.  The affidavit or other evidence is entered. An explanation of the status of the claims after entry is below or attached.

#### REQUEST FOR RECONSIDERATION/OTHER

11.  The request for reconsideration has been considered but does NOT place the application in condition for allowance because:  
See Continuation Sheet.
12.  Note the attached Information Disclosure Statement(s). (PTO/SB/08) Paper No(s). \_\_\_\_\_
13.  Other: \_\_\_\_\_.

*Deborah Crouch*

DEBORAH CROUCH  
PRIMARY EXAMINER  
GROUP 1800/1030

Continuation of 3. NOTE: Claims 55-58 newly added, are to methods of producing an antibody raises new issues, furhter related claims were originally presented but were not elected for examination.

Continuation of 11. does NOT place the application in condition for allowance because: I. Applicants argue the rejection of claim 36 under 35 USC 112, first paragraph (written description), however, claim 46 has been canceled thus, rendering instant argument moot. II. A. Applicants argue the rejection of claims 44 and 47 under 35 USC 102(e) as being incorrect because Jacobovits teach a DNA encoding the variable region of an antibody with a unique specificity and this is not the same as the variable region locus referred to in the instant claims, which contain unrearanged germline V, D and J segments and which can be rearranged in the mouse during B cell development to give rise to a plethora of different antibody specificities. This is not found pesuasive because the claimed invention encompasses a transgenic mouse having a genome comprising human heavy and light chain immunoglobulin variabel regions and mouse heavy and light chain immunoglobulin constant regions to the extent of encoding the variable region of an antibody with unique specificity hence, the art of Jacobovits is applied. Thus, the rejection of the instant claims is maintained. II. B. Applicants argue the rejection of claims 44, 47 and 53 under 35 USC 112, first paragraph 102(b) Lonberg teaches a method of generating transgenic mice which involves inactivating mouse endogenous loci and introducing human immunoglobulin loci as two separate processes and such an approach the human Ig loci would enter the mouse genome at random locations rather than at the mouse loci. This is not found persuasive because the calimed invention encompasses insertion of a human immunoglobulin locus randomly at the mosue loci to the extent the art of Lonberg is applied. Applicants further argue this homologous recombination is performed using a targeting vector containing mouse sequences flanking a selectable marker and the effect is to introduce a marker into the endogenous mouse locus rather than a human immunoglobulin locus. This is not found persusasive because the invention of Lonberg et al, relates to heavy and light chain immunoglobulin transgenes for making such transgenic non-human animals as well as methods and vectors for disrupting endogenous immunoglobulin loci in the transgenic animal to the extent a reporter gene such as a selectable marker is also encompassed by the method of Lonberg. As such the rejection of the instant claims is maintained. II. C. Applicants argue the rejection of claims 44, 47 and 53 under 35 USC 112, first paragraph 102(b) Kuncherlapati teaches alterantive strategies for producing transgenic mice with human antibodies and endogenous loci are inactivated and human loci are introduced as two separate processes. Applicants argue that the second strategy is set forth using human immunoglobulin loci to replace and inactive mouse endogenous loci in a single step but no details of a light chain locus are provided at all, much less a description of a human immunoglobulin light chain variable region locus linked to a mouse constant region locus such that hybrid locus can rearrange a chimeric antibody as claimed. Applicants further argue that use of an analogous strategy for the light chain as heavy chain would be still less likely to result in a chimeric light chain than a chimeric heavy chain because trans-switching is a heavy-chain-only phenomenon. Applicants further argue that Kuncherlapati does not mention of producing chimeric antibodies. This is not found persusasive because when the human immunoglobulin loci to replace and inactivte the variable region locus of mouse endogenous loci in a single step as taught by Kuncherlapati antibody is produced inherently its constant region is of mouse origin which renders the produced antibody chimeric.